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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,476	04/01/2004	Teresa Elisa Virgina Silva Cabezon	VU60111	1568

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
06/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,476	CABEZON ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Re: Cabezon et al

Election/Restrictions

1. Applicant's election with traverse of group I (claims 1-3 and 8-10) in the reply filed on 3/12/2007 is acknowledged. Upon further review and reconsideration, the restriction between sequences 3 and 4 is withdrawn and the two sequences will be examined together. As indicated by the applicant, the sequences of SEQ. ID No: 3 and 4 are not the invention, rather the clamed invention is drawn to an immunogenic fragment of a Cripto polypeptide which comprises at least 20 amino acids, comprises SEQ. ID No: 97, does not comprise SEQ. ID No: 11 or 12, and is "immunologically reactive" with an antibody and/or "T-cell reacts" with SEQ. ID No: 3 or 4.

2. Claims 1-7 and 11-20 are canceled without prejudice or disclaimer. Claims 8-10 are pending and examined on the merits.

Claim Rejections - 35 USC § 112, 1st paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A WRITTEN DESCRIPTION REJECTION.

The written description in this case only sets forth an immunogenic composition comprising a pharmaceutical carrier, adjuvant or immunostimulant and a Cripto fragment consisting of SEQ. ID No: 3,4,11,12, or 97 and therefore the written description is not commensurate in scope with the claims which read on compositions comprising an immunogenic fragment at least 20 contiguous amino acids in length comprising SEQ. ID No: 97, which includes a broadly un-described genus of peptides.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the claimed genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See *University of Rochester v. G.D. Searle & Co., Inc.*, F.3d, 2004 WL 260813,

at 9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of immunogenic polypeptides that encompass the structural and/or functional requirements of genus. Further, the genus are highly variant and inclusive of numerous structural variants between genus members. Further, the specification and the claims provide no guidance on structure of variants that would be immunologically reactive with a member of the group consisting of antibodies that react with a polypeptide of SEQ ID NO:3, antibodies that react with a polypeptide of SEQ ID NO:4, T-cells that react with a polypeptide of SEQ ID NO:3, and T-cells that react with a polypeptide of SEQ ID NO:4. Further, Lederman et al (Molecular Immunology 28:1171-1181) teaches that subtle differences in the sequence of a polypeptide affects the immunogenic properties of said polypeptide. Specifically, Lederman et al teaches that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Therefore, without specific guidance, one would not know exactly which polypeptides are encompassed by the claimed genera. Per the Enzo court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, a steroid couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function" and the expression of "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity and which therefore fails to satisfy the written description requirement. Similarly, the recited functional characteristics of the claimed genus does

not distinguish them from the large number of species comprising the specific structural requirements recited in the claims. The disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus are highly variant, the disclosure of the SEQ ID NOs disclosed in the specification is insufficient to describe the genus. The general knowledge and the level of skill in the art do not supplement the omitted description because specific, not general, guidance is needed.

In deciding *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997), the Federal Circuit held that a generic statement that defines a genus of nucleic acids *by only their functional activity* does not provide an adequate written description of the genus. By analogy, a generic statement that defines a genus of immunogenic fragments by only their common ability react with an antibody and or to T-cells does not serve to adequately describe the genus as whole. The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

"[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Furthermore, the Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). In this instance, as in that, there is no language that adequately describes with the requisite degree of particularity necessary to satisfy the written description requirement the genus of structurally variable polypeptides comprising at least 20 contiguous amino acids of SEQ. ID No: 97 having the claimed activities. Again, a description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Salomon *et al* (US Patent 5,264,557, issued 23 November 1993). Salomon *et al* teach a peptide that comprises at least 20 contiguous amino acids of SEQ. ID No: 97, does not

comprises either SEQ. ID No: 11 or 12. Because the peptide taught by Solomon *et al* comprises SEQ. ID No: 4 it is in the absence of evidence to the contrary capable of reacting with an antibody and or a T-cell that reacts with SEQ. ID No: 4 (see sequence alignment, below). Salomon *et al* also describe the use of KLH (see Col. 5, for example) and the use of the peptide as a immunizing agent for the generation of antibodies (see Col. 5, for example).

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  Query Match             98.6%;  Score 1033;  DB 1;  Length 188;
  Best Local Similarity   98.9%;  Pred. No. 1.6e-98;
  Matches  186;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MDCRKMVRFSYSVIWIMAISKAFELGLVAGLGHQEFARPSRGDLAFRDDSIWPQEEPAIR 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy         61 PRSSQRVLPMGIQHSKELNRTCCLNGGTCMLESFCACPPSFYGRNCEHDVRKENCGSVPH 120
              |||||||||||||||||||||||| ||||| ||||||||||||||||||||||||||||
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Qy        121 DTWLPKKCSLCKCWHGQLRCFPQAFLPGCDGLVMDEHLVASRTPELPPSARTTTFMLAGI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 DTWLPKKCSLCKCWHGQLRCFPQAFLPGCDGLVMDEHLVASRTPELPPSARTTTFMLAGI 180

Qy        181 CLSIQSYY 188
              ||||||||
Db        181 CLSIQSYY 188
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7. Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams *et al* (WO 2002/22808-A2). Williams *et al* teach an immunogenic composition comprising a pharmaceutical carrier (see page 10, for example) and a polypeptide comprising SEQ. ID No: 97, does not comprise either SEQ. ID No: 11 or 12. Because the peptide taught by Williams *et al* comprises SEQ. ID No: 4 it is in the absence of evidence to the contrary capable of reacting with an antibody and or a T-cell that reacts with SEQ. ID No: 4 (see sequence alignment, below). Williams *et al* also teach that the peptide can be attached to KLH for the generation of a Th1 response (see page 13, for example).

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  Query Match             100.0%;  Score 1048;  DB 5;  Length 188;
  Best Local Similarity   100.0%;  Pred. No. 4.7e-85;
  Matches  188;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MDCRKMVRFSYSVIWIMAISKAFELGLVAGLGHQEFARPSRGDLAFRDDSIWPQEEPAIR 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDCRKMVRFSYSVIWIMAISKAFELGLVAGLGHQEFARPSRGDLAFRDDSIWPQEEPAIR 60

Qy         61 PRSSQRVLPMGIQHSKELNRTCCLNGGTCMLESFCACPPSFYGRNCEHDVRKENCGSVPH 120
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Db         61 PRSSQRVLPMGIQHSKELNRTCCLNGGTCMLESFCACPPSFYGRNCEHDVRKENCGSVPH 120

Qy        121 DTWLPKKCSLCKCWHGQLRCFPQAFLPGCDGLVMDEHLVASRTPELPPSARTTTFMLAGI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 DTWLPKKCSLCKCWHGQLRCFPQAFLPGCDGLVMDEHLVASRTPELPPSARTTTFMLAGI 180

Qy        181 CLSIQSYY 188
              ||||||||
Db        181 CLSIQSYY 188
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Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salomon *et al* or Williams *et al* in view of Sokol *et al* (US Patent 6,270,777, issued 7 August 2001).

a. The teachings of Salomon *et al* and Williams *et al* are set forth above as they apply to claims 8-9. Salomon *et al* and Williams *et al* do not specifically teach the use of specific adjuvants. However, this deficiency is remedied by Sokol *et al.*

b. Sokol *et al* teach antibody production by purifying peptides, coupling said peptides to carrier proteins, and mixing said peptides with adjuvants to help stimulate the antigenic response of an animal (column 11 lines 63-67, in particular). Sokol *et al* further teaches the immunogenicity of antigens can be significantly improved if they are co-administered with adjuvants (column 9 lines 42-45, in particular). Sokol *et al* further teaches adjuvants such as MPL and QS21 enhance immune responses to the administered antigen (column 9 lines 42-48, in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Salomon *et al* or Williams *et al* with Sokol *et al* to make a immunogenic composition with adjuvants that are capable of stimulating a Th1 type response by the addition of adjuvants such as QS21 or MPL, because the prior art provides sufficient motivation to make such combinations. In particular, both Salomon *et al* and Williams *et al* teach the production and use of a peptide that comprises SEQ. ID No: 97 and does not comprise either SEQ. ID No: 11 or 12. They also teach that the peptides can be combined with KLH for the production of antibodies. Sokol *et al* teach that the administration of peptides in conjunction with adjuvants improves the immunogenicity of peptides/antigens. Therefore, those of skill in the art would be motivated to combine the two products such that there is improved

antigenicity. Moreover, the use of adjuvants such as MPL or QS21 are well known and often used in the art to help boost an immune response to peptides.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTOPHER H. YAEN
PRIMARY EXAMINER

Art Unit 1643
May 28, 2007